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SUMMARY

A case of hypopituitarism in a woman of 71 years is described. The interesting features of this case are the rapid response to treatment and change in mentality following treatment. Although when first seen she had got to the stage where she was vomiting and lapsing into coma, she is now back home and able to enjoy a normal independent life. She is well maintained on a very small dose of cortisone.

It is felt that physicians need to be aware of the existence of cases like this. Old people should not be dismissed as arteriosclerotic and senile until all other causes of their condition have been excluded.

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CARDIAC METASTASES IN BRONCHOGENIC CARCINOMA*

GENERAL CONSIDERATIONS; REPORT OF A CASE

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FREQUENCY OF CARDIAC METASTASES

CARDIAC METASTASES are no longer curiosities. Innumerable cases have now been reported in the literature. Their real frequency is not yet known; only the macroscopic metastases found at necropsy have been reported. They may be discovered at any age, even in children.

Table I shows the frequency of cardiac metastases and number of autopsies performed, as reported by various authors. According to these authors, cardiac metastases are found in about 0.7% of autopsies.

Evidently, the frequency of cardiac metastases is higher if only malignant tumours are considered, as shown in Table II, which indicates a mean frequency of cardiac metastases in malignant tumours of about 6%.

TABLE I.—INCIDENCE OF CARDIAC METASTASES IN AUTOPSY SERIES

Year	*Authors*	*No. of autopsies*	*Percentage*
1854	Willick	1801	0.28
1891	Pic and Bret	1708	1.4
1902	Kohler and Tandson (according to Cornil)	8289	0.07
1902	Reichelmann[1]	711	1.6
1907	Bryant	2492	0.3
1908	Karrenstein	6655	0.2
1927	Nicholls	36,980	0.32
1932	Stout[2]	1171	1.2
1934	Lymburner	8550	0.6
1935	Helwig	1000	0.9
1935	Nusbaum and Heyer	23,476	0.4
1936	Pollia and Gogol	46,072	0.48
1939	Scott and Garvin	11,000	0.9
1939	Benjamin	40,000	0.5

TABLE II.—INCIDENCE OF CARDIAC METASTASES BY NUMBER OF MALIGNANT TUMOURS (MACROSCOPIC)

Year	*Authors*	*Number*	*Percentage*	
1854	Sibley and Anott	61	Cancer of breast	14.7
		44	Cancer of uterus	4.5
1896	Obermeier	111	Sarcomas	7.2
1907	Blumensohn	1078	Carcinomas	3.1
		160	Sarcomas	7.5
1909	Offergeld	7071	Cancer of uterus	0.2
1917	Symmers	298		5.4
1922	Kitani	452		1.9
1924	Bardenheurer	1275		2.8
1926	Januz	831		1.4
1930	Maxwell	161	Thoracic metastases.	13.0
1933	Siegel and Young	44		7.4
1934	Burke	327		4.3
1934	Willis[3]	323		6.2
1939	Scott and Garvin	1082		10.9
1941	Ritchie	857	(16 cases)	1.8
1942	Herbut and Maisel	640	(35 cases)	8.4
1950	Dimmette	455		8.35
1951	Prichard[4]	4375		3.4
1951	Lamberta	1032	Epithelial tumours.	3.0
1953	de Loach[5]	980		13.9
1953	Bisel[6]	500		21.0

TYPE OF PRIMARY TUMOURS MORE FREQUENTLY FOLLOWED BY CARDIAC METASTASES

If malignant tumours can metastasize to the heart, how frequently does this occur in bronchogenic carcinoma? Table III shows that there is no general agreement on this point.

TABLE III.—MALIGNANT TUMOUR MOST COMMONLY ASSOCIATED WITH CARDIAC METASTASES

Year	*Authors*	*Tumour*	
1922	Kauffmann	Malignant melanoma	
1941	Reuling and Razinsky[7]	Cancer of bronchus	
1948	Raven	Cancer of breast	
1948	Hall[8]	Hypernephrosis—lymphoblastoma melanoma	
1953	Saphir[9]	Malignant melanoma	
			Per cent
1933	Ochsner and DeBakey	Cancer of bronchus	26.0
1933	Warren and Witham	Cancer of breast	4.52
1935	Jaffe	Cancer of bronchus	2.0
1939	Grauer	Cancer of pancreas	3.0
1939	Scott and Garvin	Cancer of bronchus	35.6
		Reticulosarcoma / Lymphoid leukæmia / Melanoma	50.0
1943	Davidson	Cancer of bronchus	10.0
1951	McMillan	Cancer of bronchus	8.0
1953	Bisel[6]	Malignant melanoma	44.0
		Cancer of breast	33.0
		Cancer of lung	31.0
		Lymphoma	24.0

*From the Departments of Medicine and of Pathology, St. Sacrement Hospital, Quebec City. Read at the 89th Annual Meeting of the Canadian Medical Association, Quebec City, June 13, 1956.

TABLE IV.—PART OF HEART MOST COMMONLY INVOLVED

Left			*Right*		
1934	Burke	Out of 14 cases	1927	Kirch	
1935	Willis[11]	20	1931	Yater	
1939	Scott and Garvin	79	1934	Lymburner	Out of 51 cases
			1945	Mahaim[10]	
			1951	Prichard[4]	150
			1953	de Loach[5]	137
	Either			*Ventricular*	
1927	Morris		1934	Willis[3]	Out of 42 cases
1942	Herbut and Maisel		1939	Scott and Garvin	79

From this study, one may conclude that the malignancies which more frequently metastasize to the heart are bronchogenic carcinoma, breast carcinoma, melanosarcoma and lymphomas, with a frequency of about 25% to 30%.

CARDIAC LOCALIZATION OF METASTASES

It is frequently stated that metastases are commoner in the right side of the heart, but this is far from being accepted by all. However, every author agrees that cardiac metastases are more often located in the ventricles than in the auricles.

SYMPTOMATOLOGY

According to Mahaim,[10] the lack of interest in the symptomatology of cardiac metastases is to be deplored. Certain primary tumours of the heart and the pericardium are operable, while others might be benefited by roentgen therapy. Moreover, in intrathoracic tumours and in bronchogenic carcinoma amenable to surgery, it is important to know in advance whether or not the heart has been invaded by the primary neoplasm. Indeed, surgery is contraindicated if a positive diagnosis of cardiac invasion is made.

Silent metastases

The symptomatology of cardiac metastases is extremely variable, and is usually less the result of their size than of their location.[10] This is well demonstrated by the fact that in certain cases, where metastases have extensively replaced the myocardium, there are almost no symptoms. Thus, metastases may be clinically silent, not giving rise to any sign of actual heart disease.

In the series of 106 cases of cardiac metastases reported by Bisel and his associates,[6] secondary invasion of the heart was associated with symptoms and physical signs of heart disease in only 8.5%. There was no parallelism between the extent of cardiac metastases and the clinical manifestations.

Metastases with signs of heart failure

At other times, the clinical picture may be one of the usual congestive failure. In fact, these cases are not strictly silent, although the clinical signs are not specific. If, in a particular case, the heart failure is not readily explained by the usual underlying pathology of cardiac insufficiency, the possibility of secondary cardiac invasion has to be considered, especially in a patient known to have cancer.

Metastases with signs of pericardial invasion

However, if there is a particular location of the metastatic tumour, more specific signs of cardiac impairment may supervene. For instance, pericardial infiltration may be followed by neoplastic adhesions with the usual consequences. Friction rubs or signs of pericardial effusion may appear. Moreover, there are cases where malignant cells have been detected in the pericardial fluid, making possible a positive diagnosis of neoplastic invasion of the pericardium.

Metastases with arrhythmias

As far as symptoms are concerned, the arryhthmias are particularly likely to attract attention. For instance, fibrillation or a flutter will suggest the possibility of a secondary auricular invasion.

A very slow pulse will be of great diagnostic value. A case is reported by Rosler[12] in which a clinical diagnosis of septal metastasis had been made because of a pulse rate of 26-28 per minute. The primary cancer was located in the skin of the cheeks. More recently, a case of auriculo-ventricular block was published by Reuling and Razinsky.[7] The septal metastasis was

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secondary to a bronchogenic carcinoma. However, these septal metastases are exceptional and are almost curiosities.[10] They are not always and necessarily followed by arrhythmias; in fact, in some reports septal metastases found at autopsy had not given rise to any symptoms suggesting such a localization during the patient's life.

If the septum is involved, one branch only of the bundle of His may be destroyed, and this will be revealed by the electrocardiogram without any other clinical symptom. Such a case was reported by Willius and Amberg.[13]

In the arrhythmic cases, a distinction has to be made between those which develop with intrathoracic and extrathoracic tumours. With the arrhythmias accompanying an intrathoracic tumour, the defect in conduction is not necessarily due to a metastatic destruction of the myocardium, but may be the result of invasion and irritation of regulatory extracardiac nerves. In these cases, the arrhythmia is only an accidental and initial finding, and will disappear when the nerves are destroyed. Paull and his associates[14] have published a case of this kind where a sinus bradycardia and syncope were the presenting signs of a bronchogenic carcinoma. The right vagus nerve was compressed by hypertrophied mediastinal nodes. On the contrary, in the case of extrathoracic tumours, it is reasonable to believe that an arrhythmia or auriculo-ventricular block is the result of a septal metastasis brought through the coronary circulation. In these cases, the metastatic destruction is permanent, and the block also is durable and definitive.

Metastases with angina pectoris

Finally, as myocardial metastases are brought to the heart by the coronary arteries, they may produce a picture of angina pectoris, simulating coronary thrombosis. Kapsinow[15] reported a fatal case of angina pectoris in which a compression of the coronary arteries by myocardial metastases originating from a breast carcinoma was found at autopsy.

Metastases and electrocardiographic findings

Although cardiac metastases may remain clinically silent, there may be electrocardiographic signs suggesting the presence of cardiac disorders; indeed, they are present more often than the clinical signs. In the statistics of Bisel and his associates,[6] electrocardiographic findings were present in 28.8% of cases. They were represented by anomalies of the T wave, low voltage of the QRS complex, ST segment deviations, abnormal Q waves, prolonged P-R interval and arrhythmias.

A 61-year-old white mechanic was admitted to hospital on June 9, 1956, after loss of consciousness preceded and followed by slight dyspnœa and by substernal and constrictive pain which had lasted all night and the day after.

The patient—whose family history was not contributory except for the fact that his father died of carcinoma of the stomach—was "very well" until April 1955, when, after a "bad cold" of a few days' duration, he experienced for the first time anginal pain and slight dyspnœa on exertion. Cough and expectoration were

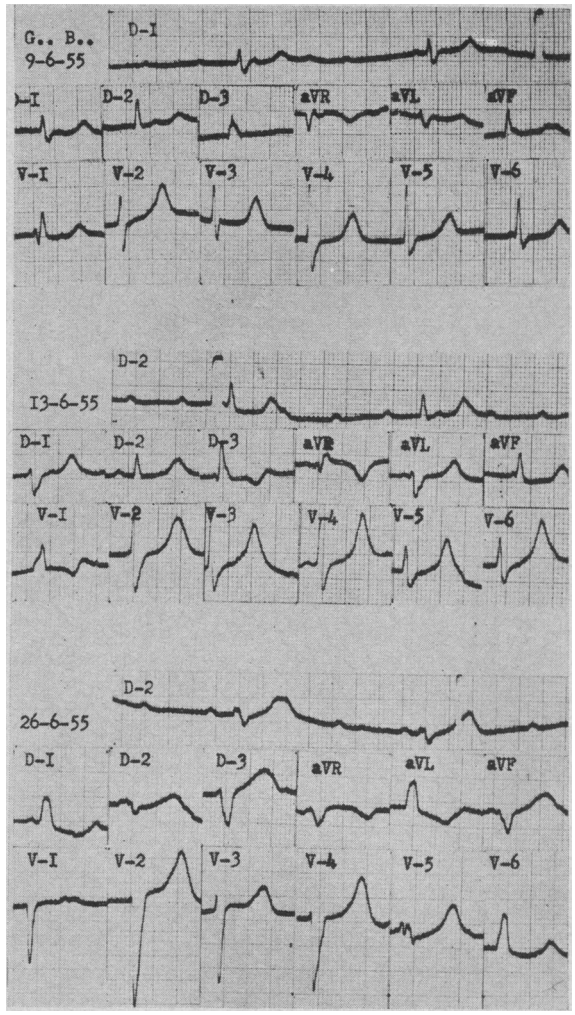


Fig. 1

only slight. Because of anginal and rheumatic pains and because of an intractable supraorbital neuralgia, this patient had been absent from work since April 1955.

The first time we saw him, he was acutely ill, anxious, dyspnœic and practically unable to move. Both heart sounds were weak and regular. Congestive rales were present at both lung bases. The pulse rate was 40, the blood pressure 120/55 mm. Hg, the rectal temperature 102° F. The physical examination was otherwise negative.

Our preliminary clinical diagnosis was one of myocardial infarct involving the septum, because of the heart block. The patient was treated accordingly.

The day after (June 10) urinalysis was normal. Examination of the blood showed a red cell count of 4,380,000, a hæmoglobin level of 11 g. % and a white cell count of 20,600 with a normal differential count. The blood urea was 1.72 g. per 1000 c.c. and the Wassermann test negative.

Three consecutive electrocardiographic tracings are intriguing. The first, made on June 10 (when the blood urea was 1.72 g. per 1000 c.c.), showed a third-degree atrioventricular block with a regular ventricular rhythm at 40 and auricular rhythm at 110 per minute. Although a pattern of right bundle branch block was present, this diagnosis was untenable without a previous tracing in sinus rhythm. This ECG was characteristic of complete A-V block with idioventricular rhythm, the pacemaker being located on or adjacent to the left main stem bundle. There were no obvious signs of myocardial infarct.

The second, made on June 13 (at that time the blood urea had dropped to 0.48 g. per 1000 c.c.), was a still better illustration of the same pattern as far as the right bundle branch block was concerned. This tracing still showed a complete A-V block with a ventricular rhythm of 37 per minute. Although the T waves on the precordium were taller and more sharply pointed, the obvious signs of myocardial infarct were still lacking.

typhoid antigens O, H, paratyphoid A and B and brucellosis were all negative. Repeated blood cultures were negative. The hæmoglobin level on July 7 was 9 g. per 100 c.c. of blood and the red cell count 4,000,000. Blood urea was 1.72 g. per 1000 c.c. on the first day in hospital, and successively 0.23 g., 0.25 g. and finally 1.55 g. in the last few days. Diarrhœa was slight and intermittent.

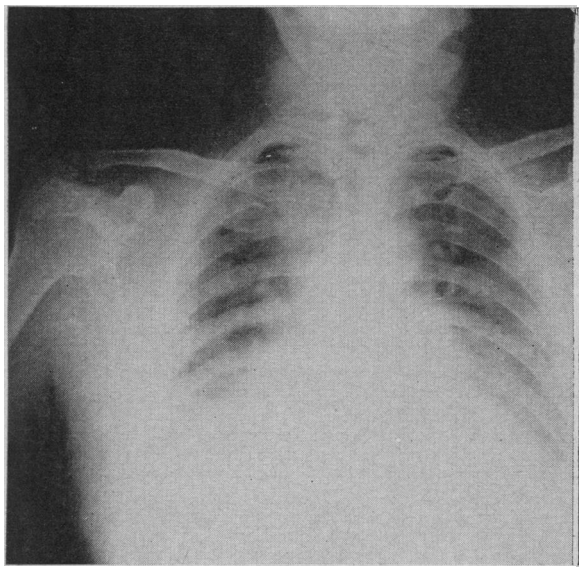


Fig. 2

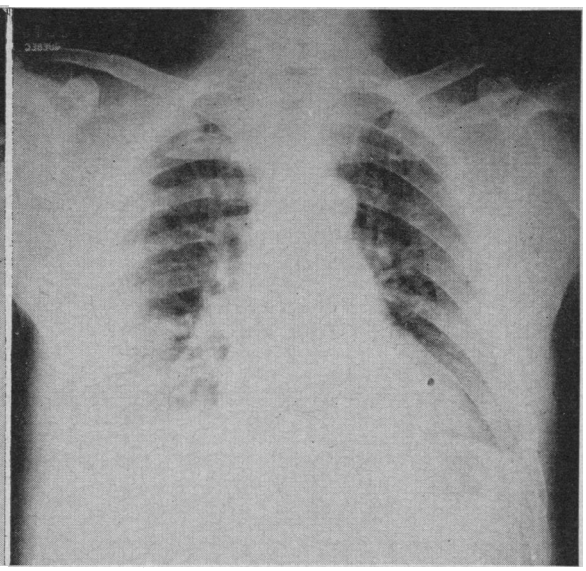
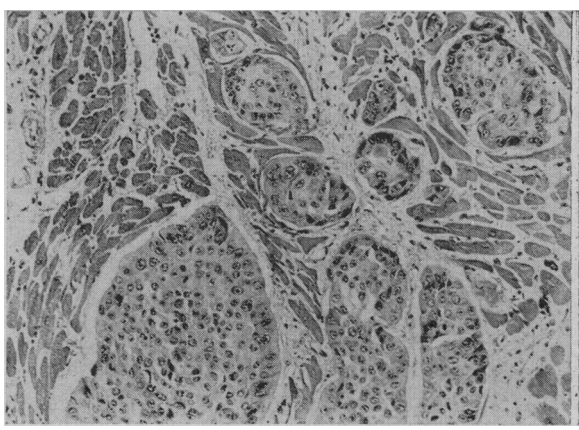


Fig. 3

On the third one, made on June 26 (at that time the blood urea was 0.23 g. per 1000 c.c.), the third-degree A-V block was still present at a ventricular rhythm of 38, but the QRS complex of the right bundle branch block pattern in the two previous tracings was now one of left bundle branch block type. This sudden change in location of the pacemaker is perhaps suggestive of a complete destruction of both right and left main bundles.

Pulmonary rales were constantly present at both lung bases but cough was consistently slight and sputum scanty. However, sputum examination showed staphylococci and pneumococci. There was no *Candida albicans*.

In a roentgenogram of the chest made on June 14 at the bedside, respiratory motion obscured details of the lung fields. Another film, made on July 1 with the patient in a sitting position, was read: "Multiple diffuse shadows throughout both lower lung fields, more



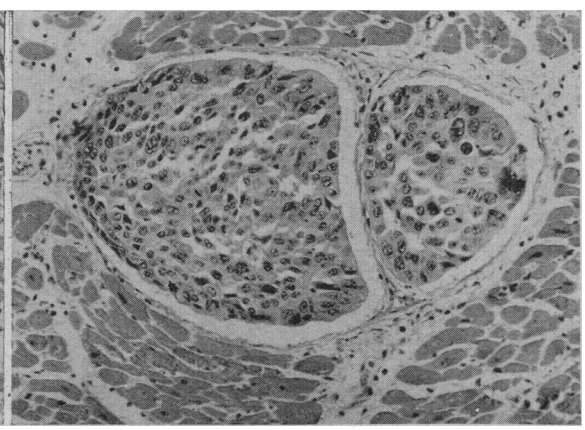


Fig. 4.—Heart: myocardium—nodular metastases from a bronchogenic carcinoma. Fig. 5.—Heart: myocardium—nodular metastases from a bronchogenic carcinoma. Note the compression of the myocardial fibres by these metastases.

The patient was acutely ill during the whole course of his illness. The rectal temperature remained high, except for a few days, in spite of an intensive course of many and various antibiotics (Achromycin, terramycin, erythromycin, penicillin, streptomycin). The sedimentation rate was 61 mm. in one hour on June 27 and 86 mm. on July 13. The serological agglutination tests for

accentuated on the right side. Increased lung markings throughout the remaining lung fields". The patient was too sick to have a lateral view taken.

In July the cardiovascular status was still the same. The blood pressure was nearly always 140/70. He often had the same constrictive substernal pain radiating to the right shoulder.

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During his 57 days in hospital, the patient, always acutely ill, suffered an intractable supraorbital neuralgia with hemicrania on the left side; because of an iridocyclitis, the fundus was difficult to see and it was only later that detachment of the retina could be seen.

At the end of July, neurological manifestations were predominant with exophthalmos and facial palsy on the left side and hemiplegia on the right. The patient was mentally confused. The cerebrospinal fluid showed normal cytology but the albumin was 1.10 g. per 1000 c.c.

In his last days the patient suffered from frequent Adams-Stokes attacks. He did not survive the last one and died on August 4.

The important points in this case were:

1. An episode of supraorbital neuralgia,
2. Adams-Stokes attacks with anginal pain initially considered the result of a myocardial infarct unproved by electrocardiograms.
3. Constant predominance of a febrile illness of unknown origin during the whole course of the disease.
4. At the end a well-developed neurological syndrome.
5. No clinical picture of a primary pulmonary disease.

The *post-mortem examination* was performed two hours after death.

A whitish nodule 9 mm. in diameter was attached to the internal aspect of the dura mater, and compressed the underlying brain substance. There was a 5 x 22 mm. tumour in the left eye, between the retina and the choroid.

The left lung weighed 410 g., and its lower lobe contained a white mass, partially necrotic, whose diameter was 7 cm. This neoplasm was surrounded by many nodules of the same nature.

The heart was of normal weight; the pericardial cavity was free of excess of fluid, and the pericardium itself was without abnormalities. In the anterior wall of the left ventricle there was a small white nodule. The superior part of the interventricular septum contained a neoplastic metastasis of 3 cm. diameter. This mass involved the whole thickness of the septum. The coronary arteries were normal.

There was an ulceration of the jejunum. The liver showed no macroscopical abnormalities.

On microscopic examination the broncho-pulmonary neoplasm was seen to be a keratotic squamous-cell carcinoma (epidermoid carcinoma). The dura mater nodule, the left ocular tumour, the nodules in the myocardium and the jejunal ulceration were composed of the same cells and were metastases from the bronchogenic carcinoma. In the liver, one small portal vessel was filled with carcinomatous cells.

DISCUSSION

This case report indicates once more that, although it is relatively easy to suspect the presence of a cardiac metastasis in an obvious case of cancer, it is rather difficult to make such a diagnosis when the primary tumour is unknown.

This case report gave us occasion to read most of the literature on the subject, and we have found that some authors emphasize the relatively high incidence of cardiac metastases in bronchogenic carcinoma. In the latest paper written on the subject (April 1956) Le Gal and Rouillard[16] reported 10 cases of cardiac metastases, four of which were secondary to bronchogenic carcinoma, an incidence of 40%.

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CLINICO-PATHOLOGICAL CONFERENCE. IX.

MONTREAL GENERAL HOSPITAL
NOVEMBER 15, 1956

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Montreal

A 45-YEAR-OLD WHITE MAN was admitted, on March 19, 1956, to the surgical private patients' pavilion because of abdominal pain, nausea and vomiting, loss of appetite, weight loss and the passage of blood per rectum.

First admission.—The patient had been admitted to the Medical Service five months previously. For 10 years he had had multiple gastro-intestinal symptoms. At the onset he had had intermittent abdominal pain of variable quality on either side of the abdomen at the level of the umbilicus. The pain was accompanied by nausea and vomiting which occurred almost daily. The patient also suffered intermittent alternate diarhœa and constipation. The stools were occasionally very dark but not tarry. He had no particular food intolerance. At the onset—10 years before—the patient had barium series and enema, which were negative. A friend recommended Isogel, which the patient took with much relief of symptoms. However, in the past month his pain, nausea and vomiting recurred. He had lost 2-3 lb. in weight.

Physical examination revealed a somewhat distended and tense abdomen with moderate tenderness—but no masses—in both lower quadrants. Rectal examination was negative. A barium series revealed an initial pylorospasm the significance of which by itself was doubtful. Barium